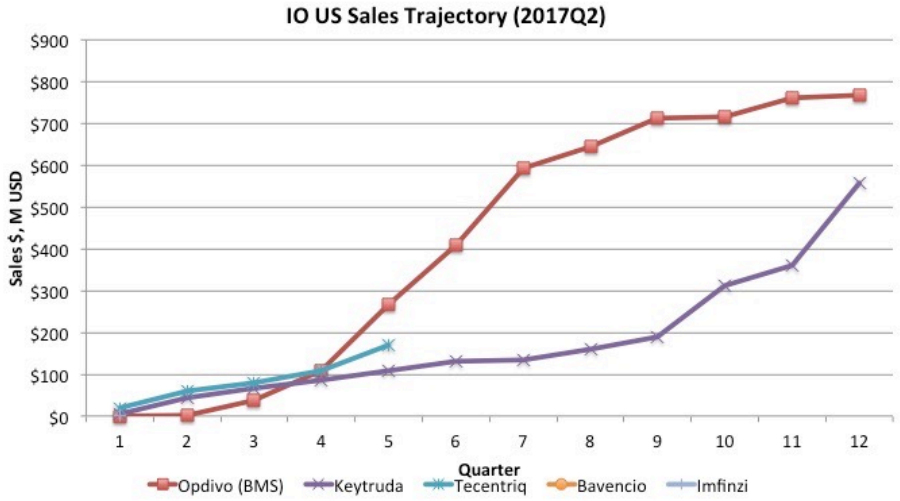
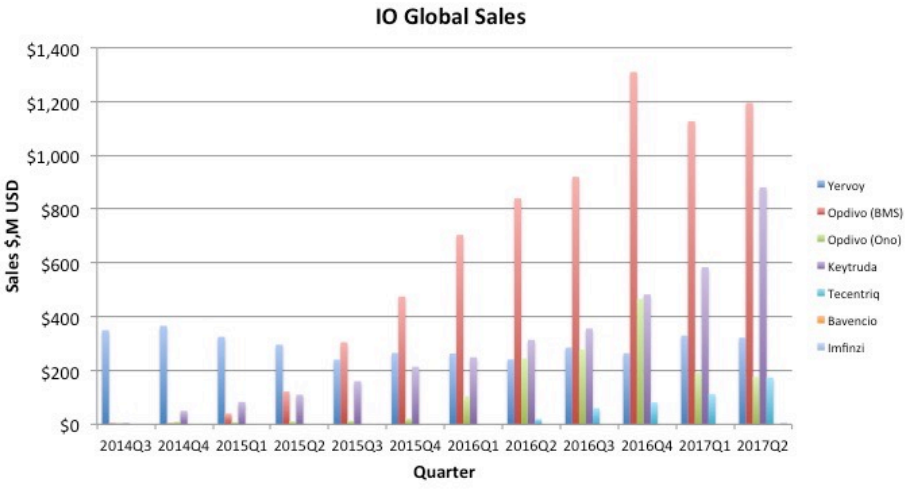
The Immuno-Oncology Race: Recent Successes and Failures

Boulder, Colorado, September 12, 2017 -- Three years on, there continues to be much excitement about the immuno-oncology class (IO) of cancer therapies. As of today, five agents have received regulatory clearance (for at least one indication) and a number of agents and combinations are in clinical development for a wide range of indications.

Although Opdivo (nivolumab; BMS) initially captured the largest share of market value, Keytruda (pembrolizumab; Merck) is now gaining traction and showing an improved sales trajectory (see graph).



Keytruda appears to be capitalizing on Opdivo's recent clinical trial shortfalls in 1st-line lung, 1st-line lung combination with Yervoy and 1st-line renal cell carcinoma).



Unlike Opdivo, Tecentriq (atezolizumab; Roche) or Imfinzi (durvalumab; AstraZeneca), Keytruda seemed immune to clinical failures. However, Keytruda has recently stumbled in two

indications: in multiple myeloma, with a clinical hold, and in HNSCC (head and neck squamous cell carcinoma), with a failure to demonstrate an overall survival benefit (primary endpoint) versus standard treatment (methotrexate, docetaxel or cetuximab).

Agent	Trial	Indication Failure	Date Announced	References	
Opdivo	CheckMate-026	1st-line lung	2016-8-05	BMS PR 2016-8-5	
Opdivo		1st-line lung combo with Yervoy	2017-1-19	BMS PR 2017-1-19	
Opdivo, in combo w/ Yervoy	CheckMate-214	1st-line mRCC	2017-8-15	BMS PR 2017-8-15	
Tecentriq	IMvigor 211	2nd-line bladder	2017-5-10	Roche PR 2017-5-10	
Keytruda	Keynote-183	Multiple myeloma; R/R MM in combo with pomalidomide or lenalidomide	2017-6-12	Merck PR 2017-6-12	Merck PR 2017-7-5
	Keynote-185				
	Keynote-023				
Keytruda	Keynote-040	HNSCC	2017-7-24	Merck PR 2017-7-24	
Imflinzi	MYSTIC	1st-line lung combo with tremelimumab	2017-7-27	AstraZeneca PR 2017-7-27	

Given the differing clinical trial shortfalls to date across the immuno-oncology class (see table), it appears the IO agents are not all created equal. It also highlights how much the drug developers may not know about how each agent, or combination, works in different cancer indications. In the least, it shows there will be increasing differentiation based on specific indications in different cancer types or stages.

To that point, at ESMO last week, Imfinzi posted exciting results from the PACIFIC trial in the lung cancer maintenance setting (NCT-02125461).
These results in patients with stage 3, surgery-ineligible, non-small cell lung cancer showed Imfinzi halted disease progression (progression-free survival; PFS) for a median time of 16.8 months, an improvement of more than 11 months versus placebo. The PACIFIC trial results also suggest that IO agents (at least Imfinzi) may have a role in non-metastatic disease, broadening the market opportunity.

These positive results followed the shortfall from the MYSTIC trial (NCT02453282) where the combination of Imfinzi plus tremelimumab failed to show an improvement in disease progression in first-line metastatic (stage IV) non-small lung cancer versus platinum-based standard of care chemotherapy, reported by AstraZeneca.

There is much yet to unfold and to tell about the IO story. Stay tuned.